

Application No. 09/493,480  
Attorney Docket No. CRX113US

### AMENDMENTS TO THE CLAIMS

#### **In the Claims:**

1-92. (canceled)

93. (Currently amended) An isolated nucleic acid molecule encoding a polypeptide comprising a ~~HER-2/Neu fusion protein, the HER-2/Neu fusion protein consisting of:~~

- (a) ~~HER-2/Neu extracellular domain linked to an amino acid sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the HER-2/Neu extracellular domain in a warm-blooded animal; and~~
- (b) ~~a HER-2/Neu phosphorylation domain an amino acid sequence having at least 90% sequence identity to SEQ ID NO:4, and which increases the immunogenicity of (a) in a warm-blooded animal;~~

~~wherein (a) and (b) are joined by an amino acid linker sequence of no more than 50 amino acids; and wherein said polypeptide does not comprise and not comprising a HER-2/Neu transmembrane domain sequence or any portion of a HER-2/Neu intracellular domain other than the phosphorylation domain, wherein the HER-2/Neu fusion protein comprises at least 90% identity to SEQ ID NO:6 and wherein the HER-2/Neu fusion protein is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal.~~

94.-97. (canceled)

98. (Currently amended) A viral vector comprising a nucleic acid molecule of claim 93.

99. (Currently amended) A composition comprising the nucleic acid molecule of claim 93, and a physiologically acceptable carrier or diluent.

100. (previously presented) The composition of claim 99, wherein the composition is a vaccine.

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101. (previously presented) The composition of claim 99, further comprising an immunostimulatory substance.

102. (currently amended) The composition of claim 99, wherein the nucleic acid molecule is a DNA molecule.

103. (Currently amended) An isolated nucleic acid molecule encoding a polypeptide comprising a ~~HER-2/Neu fusion protein, the HER-2/Neu fusion protein consisting of:~~

(a) ~~a HER-2/Neu extracellular domain and linked to an amino acid sequence having at least 90% identity to SEQ ID NO:3 and capable of producing an immune response against the HER-2/Neu extracellular domain in a warm-blooded animal; and~~

(b) ~~a fragment of the HER-2/Neu phosphorylation domain, an amino acid sequence having at least 90% identity to SEQ ID NO: 5, and that increases the immunogenicity of (a) in a warm-blooded animal;~~

~~wherein (a) and (b) are joined by an amino acid linker sequence of no more than 50 amino acids; and wherein said polypeptide does not comprise, and not comprising a HER-2/Neu transmembrane domain sequence or any portion of a HER-2/Neu intracellular domain other than the fragment of the phosphorylation domain, wherein the HER-2/Neu fusion protein comprises at least 90% identity to SEQ ID NO:7 and wherein the protein is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal.~~

104. -107. (Cancelled)

108. (Currently amended) A viral vector comprising a nucleic acid molecule of claim 103.

109. (Currently amended) A composition comprising the nucleic acid molecule of claim 103, and a physiologically acceptable carrier or diluent.

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110. (previously presented) The composition of claim 109, wherein the composition is a vaccine.

111. (previously presented) The composition of claim 109, further comprising an immunostimulatory substance.

112. (Currently amended) The composition of claim 109, wherein the nucleic acid molecule is a DNA molecule.

113. (Currently amended) A method of making a ~~fusion~~ protein, the method comprising the steps of:

- (a) introducing into a cell an expression vector comprising a nucleic acid molecule according to claims 93 or 103;
- (b) culturing the transfected cell; and
- (c) purifying the expressed ~~fusion~~ protein.

114. (Original) The method of claim 113, wherein the cell is a CHO cell.

115. (Original) The method of claim 113, wherein the cell is cultured in suspension, under serum-free conditions.

116. (Currently amended) The method of claim 113, wherein the expressed ~~fusion~~ protein is purified by a ~~two-step procedure~~, the procedure comprising:

- (a) anion exchange chromatography; and
- (b) hydrophobic chromatography.

117. (Currently amended) The nucleic acid molecule of claim 93, wherein (a) consists of the ~~HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:3 and~~ (b) consists of ~~linked to an amino acid sequence of SEQ ID NO:4.~~

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118. (Currently amended) The nucleic acid molecule of claim 103, wherein (a) consists of 93, wherein the HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:3 and (b) consists of linked to an amino acid sequence of SEQ ID NO:5.

119. (Currently Amended) The nucleic acid of claim 117, An isolated nucleic acid molecule encoding a polypeptide comprising wherein the HER-2/Neu fusion protein consists of an amino acid of SEQ ID NO:6.

120. (Currently Amended) The nucleic acid of claim 118, An isolated nucleic acid molecule encoding a polypeptide comprising wherein the HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:7.

121. (Currently amended) The nucleic acid molecule of claim 93, wherein the polypeptide is secreted.

122. -123. Canceled

124. (Currently amended) The nucleic acid molecule of claim 103, wherein the polypeptide is secreted.

125. (Previously presented) The composition of claim 109, comprising an oil-in-water emulsion.

126. (Previously presented) The composition of claim 125, comprising tocopherol.

127. (Previously presented) The composition of claim 111, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

128. (Previously presented) The composition of claim 111, wherein the immunostimulatory substance comprises 3D-MPL and QS21 in an oil-in-water emulsion.

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129. (Previously presented) The composition of claim 128, comprising tocopherol.

130. (Previously presented) The composition of claim 109, comprising a CpG-containing oligonucleotide.

131. (New) An isolated nucleic acid molecule encoding a polypeptide comprising:

- (a) a sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the human HER-2/Neu extracellular domain in a warm-blooded animal; and
- (b) a sequence having at least 90% sequence identity to SEQ ID NO:4, and which increases the immunogenicity of (a) in a warm-blooded animal; wherein the sequences of (a) and (b) are directly linked via a peptide bond.

132. (New) A viral vector comprising a nucleic acid molecule of claim 131.

133. (New) A composition comprising the nucleic acid molecule of claim 131 and a physiologically acceptable carrier or diluent.

134. (New) The composition of claim 133, wherein the composition is a vaccine.

135. (New) The composition of claim 133, further comprising an immunostimulatory substance.

136. (New) The composition of claim 133, wherein the nucleic acid molecule is a DNA molecule.

137. (New) The nucleic acid molecule of claim 131, wherein the polypeptide is secreted.

138. (New) The composition of claim 133, comprising an oil-in-water emulsion.

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139. (New) The composition of claim 135, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

140. (New) The composition of claim 133, further comprising a CpG-containing oligonucleotide.

141. (New) An isolated nucleic acid molecule encoding a polypeptide comprising:  
(c) a sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the human HER-2/Ncu extracellular domain in a warm-blooded animal; and  
(d) a sequence having at least 90% sequence identity to SEQ ID NO:5, and which increases the immunogenicity of (a) in a warm-blooded animal;  
wherein the sequences of (a) and (b) are directly linked via a peptide bond.

142. (New) A viral vector comprising a nucleic acid molecule of claim 141.

143. (New) A composition comprising the nucleic acid molecule of claim 141 and a physiologically acceptable carrier or diluent.

144. (New) The composition of claim 143, wherein the composition is a vaccine.

145. (New) The composition of claim 143, further comprising an immunostimulatory substance.

146. (New) The composition of claim 143, wherein the nucleic acid molecule is a DNA molecule.

147. (New) The nucleic acid molecule of claim 141, wherein the polypeptide is secreted.

148. (New) The composition of claim 143, comprising an oil-in-water emulsion.

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149. (New) The composition of claim 145, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

150. (New) The composition of claim 143, further comprising a CpG-containing oligonucleotide.

151. (New) A method of making a protein, the method comprising the steps of:

- (a) introducing into a cell an expression vector comprising a nucleic acid molecule according to claim 131 or claim 141;
- (b) culturing the transfected cell; and
- (c) purifying the expressed protein.

152. (New) The method of claim 151, wherein the cell is a CHO cell.

153. (New) The method of claim 151, wherein the cell is cultured in suspension, under serum-free conditions.

154. (New) The method of claim 151, wherein the expressed protein is purified by a procedure comprising:

- (a) anion exchange chromatography; and
- (b) hydrophobic chromatography.

155. (New) The composition of claim 99, comprising an oil-in-water emulsion.

156. (New) The composition of claim 101, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

157. (New) The composition of claim 99, further comprising a CpG-containing oligonucleotide.